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Associations among lead dose biomarkers, uric acid, and renal function in Korean lead workers

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Abbreviations

BUN, blood urea nitrogen; BMI, body mass index; CV, coefficient of variation; DMSA, dimercaptosuccinic acid; EDTA, calcium disodium ethylenediamine tetraacetic acid; NAG, N-acetyl-β-D-glucosaminidase; NO, nitric oxide; RBP, retinol-binding protein; SD, standard deviation

ABSTRACT

Recent research suggests that both uric acid and lead may be nephrotoxic at lower levels than previously recognized. Data from 803 current and former lead workers were analyzed to determine whether lead biomarkers were associated with uric acid and whether previously reported associations between lead dose and renal outcomes were altered after adjustment for uric acid. Outcomes included uric acid, blood urea nitrogen, serum creatinine, measured and calculated creatinine clearances, and urinary N-acetyl-β-D-glucosaminidase (NAG) and retinol-binding protein. Mean (SD) uric acid, tibia lead, and blood lead levels were 4.8 (1.2) mg/dl, 37.2 (40.4) μg/g bone mineral, and 32.0 (15.0) μg/dl, respectively. None of the lead measures (tibia, blood, and dimercaptosuccinic acid chelatable lead) was associated with uric acid, after adjustment for age, gender, body mass index, and alcohol use. However, when effect modification by age on these relations was examined, both blood and tibia lead were significantly associated ($\beta = 0.0111$; $p < 0.01$ and $\beta = 0.0036$; $p = 0.04$, respectively) in participants in the oldest age tertile. These associations decreased after adjustment for blood pressure and renal function, although blood lead remained significantly associated with uric acid ($\beta = 0.0156$; $p = 0.01$) when the population was restricted to the oldest tertile of workers with serum creatinine greater than the median (0.86 mg/dl). Next, in models of renal function in all workers, uric acid was significantly ($p < 0.05$) associated with all renal outcomes except NAG. Finally, in the oldest tertile of workers, associations between lead dose and NAG were unchanged, but fewer associations between the lead biomarkers and the clinical renal outcomes remained significant ($p \leq 0.05$) following adjustment for uric acid. In conclusion, our data suggest that older workers comprise a susceptible population for increased uric acid due to lead. Uric acid may be one, but not the only, mechanism for lead-related nephrotoxicity.